

It is claimed:

1. A BIV combination vector construct comprising:
 - a) a DNA segment from a BIV genome, wherein the DNA segment comprises a gag gene, a pol gene, a segment of the env gene, and a BIV packaging sequence to package BIV RNA into virions;
 - b) a promoter operably linked to the DNA segment; and
 - c) a transgene operably linked to said promoter wherein the transgene is inserted into the segment of the env gene.
2. The BIV combination construct of claim 1 wherein a section of the env gene segment is deleted and the transgene is inserted into the gap created by said deletion.
3. The BIV combination construct of claim 1 wherein the promoter is a LTR promoter.
4. The BIV combination construct of claim 1 wherein the DNA segment further comprises tat and rev exons.
5. The BIV combination construct of claim 1 wherein the DNA segment further comprises tat and rev exons and the transgene is inserted between the tat and rev exons.
6. The BIV combination construct of claim 1 further comprising a rev gene.
7. The BIV combination construct of claim 1 wherein the transgene is operably linked to a second promoter.
8. A BIV vector construct comprising:
 - a) a DNA segment from a BIV genome,
 - b) a packaging sequence to package RNA into virions;
 - c) a first promoter operably linked to the DNA segment; and
 - d) a transgene operably linked to a second promoter.

9. The BIV vector construct of claim 8 wherein the packaging sequence is a BIV packaging sequence.
10. The BIV vector construct of claim 8 wherein said first promoter is a LTR promoter.
11. The BIV vector construct of claim 8 wherein said first promoter is a CMV promoter.
12. The BIV vector construct of claim 8 wherein the transgene is operably linked to a CMV promoter, a PGK promoter, or a MND promoter.
13. The BIV vector construct of claim 8 wherein the DNA segment further comprises a portion of a gag gene.
14. The BIV vector construct of claim 8 wherein the DNA segment from said BIV genome further includes gag and pol genes and a BIV packaging sequence.
15. The BIV vector construct of claim 8 further comprising a rev-response element (RRE).
16. The BIV vector construct of claim 8 further comprising a human interferon-beta scaffold attachment region (SAR).
17. The BIV vector construct of claim 8 further comprising a central polypurine tract (cPPT).
18. The BIV vector construct of claim 8 wherein the transgene is operably linked to a second promoter which is located downstream of the putative BIV RRE.
19. The BIV vector construct of claim 8 wherein a portion of the U3 region of the 3' LTR is deleted or replaced by a heterologous sequence.
20. A method of producing a BIV packaging cell line which comprises transforming an established cell line with the BIV combination vector construct of claim 1.

21. The method of claim 20 wherein the established cell line is a mammalian cell line.
22. The method of claim 21 wherein the mammalian cell line is a human cell line.
23. A BIV packaging construct comprising: a BIV DNA sequence fragment comprising at least a gag or pol gene of BIV; and a promoter operably linked to the BIV DNA fragment.
24. The BIV construct of claim 23 further comprising an internal ribosome binding site.
25. The BIV construct of claim 23 further comprising a heterologous intron.
26. A BIV packaging cell line which comprises an established cell line transformed by the BIV construct of claim 23.
27. A three vector system comprising:
 - a) a BIV vector construct comprising,
 - i) a DNA segment from a BIV genome,
 - ii) a packaging sequence necessary to package RNA into virions;
 - iii) a promoter operably linked to the DNA segment; and
 - iv) a transgene operably linked to a second promoter;
 - b) a BIV packaging vector construct comprising
 - i) a BIV DNA sequence fragment comprising at least a gag gene and pol gene of BIV;
 - ii) a promoter operably linked to the BIV DNA fragment; and
 - iii) a polyadenylation sequence located downstream of the BIV DNA fragment; and
 - c) an expression vector construct comprising a gene encoding a viral surface protein.
28. The three vector system of claim 27 wherein expression vector construct is a vesicular stomatitis virus (VSV)-G envelope glycoprotein expression vector.
29. The three vector system of claim 27 further comprising a BIV gene selected from the

group consisting of gag, vif, vpw, vpy, tat, rev, and env in the DNA segment of the first vector construct.

30. A cell line transfected with the three vector system of claim 27 said cell line being capable of producing virion particles.
31. A method of transferring a gene of interest to a mammalian cell comprising: transfecting a eukaryotic host cell with the three vector system of claim 27; culturing the transfected host cell and collecting the virions produced; and administering the collected virions to a mammalian cell to allow infection of the mammalian cell and thereby transferring the gene of interest.
32. The method of claim 31 wherein the mammalian cell is located *in vitro*.
33. The method of claim 31 wherein the mammalian cell is located *in vivo*.
34. A two vector system comprising:
 - a) BIV combination vector construct which comprises a DNA segment from a BIV genome, wherein the DNA segment comprises a gag gene, a pol gene, a segment of the env gene, and a BIV packaging sequence to package BIV RNA into virions; a promoter operably linked to the DNA segment; and a transgene operably linked to said promoter wherein the transgene is inserted into the segment of the env gene, and
 - b) a viral surface protein expression vector.
35. The two vector system according to claim 34 wherein the viral surface protein expression vector is a vesicular stomatitis virus (VSV)-G envelope glycoprotein expression vector.
36. A cell line transfected with the two vector system of claim 34.
37. A method of transferring a gene of interest to a mammalian cell comprising, (a) transfecting a eukaryotic host cell with the two vector system of claim 34; (b) culturing the transfected host cell and collecting the virions produced; and (c)

administering the virions to a mammalian cell to allow infection of said cell and thereby transfer of the gene of interest.

38. The virion particle obtained by the method of claim 37.

39. The mammalian cell infected with the virion particle of claim 37.

40. A vector construct comprising:

a promoter linked to a first BIV R region;

a BIV U5 element linked to the first BIV R region;

a packaging sequence;

a transgene; and

a BIV U3 element linked to a second BIV R region, wherein the promoter initiates RNA transcription of the vector construct.

41. The vector construct of claim 40, wherein the transgene is operably linked to an internal promoter.

42. The vector construct of claim 41, wherein one or more nucleotide sequences in the U3 element are mutated or deleted in order to diminish or eliminate U3-mediated transcription.

43. The vector construct of claim 42, wherein the packaging sequence is a BIV packaging sequence.

44. The vector construct of claim 43, wherein any start codons in the packaging sequence are eliminated by deletion or mutation.

45. The vector construct of claim 43, wherein the U3 element further comprises a sequence that enhances polyadenylation.

46. The vector construct of claim 43, wherein the major splice donor site has been inactivated or eliminated.

47. The vector construct of claim 43, further comprising a cPPT.
48. The vector construct of claim 47, wherein the cPPT is a BIV cPPT.
- 5 49. The vector construct of claim 43, further comprising a 3' polypurine tract.
50. The vector construct of claim 43, further comprising an RNA transport element.
- 10 51. The vector construct of claim 50, wherein the RNA transport element is a lentiviral rev response element (RRE).
52. The vector construct of claim 51, wherein the lentiviral RRE is a BIV RRE.
- 15 53. The vector construct of claim 50, wherein the RNA transport element is a constitutive transport element (CTE).
- 20 54. The vector construct of claim 53, wherein the CTE is a Mason-Pfizer Monkey Virus CTE.
55. A packaging construct comprising:
- a promoter operatively linked to a BIV gag/pol coding sequence; and
- a polyadenylation signal at the 3' end of the gag/pol coding sequence.
- 25 56. The packaging construct of claim 55, further comprising an intron upstream of the gag/pol coding sequence.
57. The packaging construct of claim 55, further comprising an RNA transport element.
- 30 58. The packing construct of claim 57, wherein the RNA transport element is a lentiviral RRE.
59. The packaging construct of claim 58, wherein the lentiviral RRE is a BIV RRE.

60. The packaging construct of claim 57, wherein the RNA transport element is a CTE.

61. The packaging construct of claim 60, wherein the CTE is a Mason-Pfizer Monkey Virus CTE.

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62. The packaging construct of claim 58, further comprising a Rev coding sequence.

63. A viral surface protein expression construct comprising:

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a promoter operatively linked to a viral envelope coding sequence; and
a polyadenylation signal at the 3' end of the viral envelope coding sequence.

64. The viral surface protein expression construct of claim 63, further comprising an intron between the promoter and the coding sequence.

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65. The viral surface protein expression construct of claim 63, wherein the viral envelope comprises the VSV-G virus envelope.

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66. A packaging cell comprising the packaging construct of claim 55 and the viral surface protein expression construct of claim 63.

67. A packaging cell comprising:

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a BIV gag/pol coding sequence; and
a viral envelope coding sequence.

68. The packaging cell of claim 67, further comprising an RNA transport element.

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69. The packaging cell of claim 68, wherein the RNA transport element is a lentiviral RRE.

70. The packaging cell of claim 69, further comprising a Rev coding sequence.

71. A producer cell comprising the packaging cell of claim 66 and the vector construct of claim 40.
72. A producer cell comprising:
 - a BIV gag/pol coding sequence;
 - a viral envelope coding sequence; and
 - a vector construct comprising a promoter linked to a first BIV R region, a BIV U5 element linked to the first BIV R region, a packaging sequence, a transgene, and a BIV U3 element linked to a second BIV R region, wherein the promoter initiates RNA transcription of the vector construct.
73. A virion produced by the producer cell of claim 72.
74. A method of making a packaging cell comprising the steps of:
 - transfecting a cell with a BIV gag/pol coding sequence; and
 - transfecting the cell with a viral envelope coding sequence.
75. The method of claim 74, wherein the cell is a mammalian cell.
76. The method of claim 75, wherein the mammalian cell is a human cell.
77. A method of making a producer cell comprising transfecting the packaging cell of claim 74 with the vector construct of claim 40.
78. A method of transferring a gene to a mammalian cell comprising administering the vector construct of claim 40 to said cell.
79. A method of transferring a gene to a mammalian cell comprising administering the virion of claim 73 to the cell.
80. A virion comprising an RNA vector, said RNA vector comprising a first BIV R region linked to a BIV U5 element, a packaging sequence, a transgene operably linked to a promoter, and a BIV U3 element linked to a second BIV R region.